

CLAIMS

1. An apparatus, comprising:
 - a chip comprising a predetermined reaction site having a volume of less than about 1 ml; and
 - an active control system able to control an environmental factor associated with the chip in response to a signal indicative of a condition associated with the chip, so as to support a living cell within the predetermined reaction site.
2. The apparatus of claim 1, the chip comprising a plurality of reactors, wherein one of the plurality of reactors comprises the predetermined reaction site.
3. The apparatus of claim 1, wherein the active control system is integrally connected to the chip.
4. The apparatus of claim 1, wherein the predetermined reaction site has a volume of less than about 500 microliters.
5. The apparatus of claim 1, wherein the predetermined reaction site has a volume of less than about 100 microliters.
6. The apparatus of claim 1, wherein the predetermined reaction site has a volume of less than about 10 microliters.
7. The apparatus of claim 1, wherein the predetermined reaction site has a volume of less than about 1 microliter.
8. The apparatus of claim 1, wherein the predetermined reaction site has a maximum dimension of less than about 1 cm.
9. The apparatus of claim 1, wherein the predetermined reaction site has a maximum dimension of less than about 1 mm.

10. The apparatus of claim 1, wherein the predetermined reaction site has a maximum dimension of less than about 100 micrometers.
- 5 11. The apparatus of claim 1, wherein the predetermined reaction site has a maximum dimension of less than about 10 micrometers.
12. The apparatus of claim 1, wherein at least one surface of the predetermined reaction site comprises an inorganic material.
- 10 13. The apparatus of claim 12, wherein the inorganic material comprises a semiconductor.
14. The apparatus of claim 12, wherein the inorganic material comprises a metal.
- 15 15. The apparatus of claim 1, wherein the living cell is a mammalian cell.
16. The apparatus of claim 1, wherein the living cell is a bacterium.
- 20 17. The apparatus of claim 1, wherein the cell is a plant cell.
18. The apparatus of claim 1, wherein the living cell is part of a tissue culture.
19. The apparatus of claim 1, wherein at least one surface of the predetermined reaction site comprises a polymer.
- 25 20. The apparatus of claim 19, wherein the at least one surface consists essentially of the polymer.
- 30 21. The apparatus of claim 19, wherein the polymer is selected from the group consisting of a silicone, a polycarbonate, a polyethylene, a polypropylene, a polytetrafluoroethylene, a polyvinylidene chloride, a bis-benzocyclobutene, a

polystyrene, a polyacrylate, a polymethacrylate, a polyimide, and combinations thereof.

22. The apparatus of claim 1, wherein the control system is able to control at least one
5 environmental factor within the predetermined reaction site selected from the group
consisting of:
- | | |
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| relative humidity, | pH, |
| molarity, | a concentration of a dissolved gas, |
| osmolarity, | glucose concentration, |
| 10 glutamine concentration, | pyruvate concentration, |
| apatite concentration, | color, |
| turbidity, | viscosity, |
| a concentration of an amino acid, | a concentration of a vitamin, |
| 15 a concentration of a hormone, | serum concentration, |
| a concentration of an ion, | shear rate, |
| degree of agitation, | temperature, |
| pressure, | O ₂ concentration, |
| CO ₂ concentration, | |
| 20 and a concentration of an oligopeptide. | |
23. The apparatus of claim 1, wherein the control system is able to control the
temperature within the predetermined reaction site.
24. The apparatus of claim 1, wherein the control system is able to control the pressure
25 within the predetermined reaction site.
25. An apparatus, comprising:
- a chip comprising a predetermined reaction site having a volume of less than
about 1 ml; and
- 30 a control system able to control an environmental factor associated with the
predetermined reaction site, the environmental factor being at least one of relative
humidity, pH, dissolved O₂ concentration, dissolved CO₂ concentration, and
concentration of a media component.
- 35 26. The apparatus of claim 25, wherein the control system is integrally connected to the
chip.

27. The apparatus of claim 25, wherein the chip is constructed and arranged to maintain at least one living cell at the predetermined reaction site.
28. The apparatus of claim 25, wherein the media component is selected from the group consisting of a carbohydrate source, serum, a growth factor, an enzyme, a hormone, an amino acid, or an oligopeptide.
29. The apparatus of claim 25, wherein the carbohydrate source is glucose.
30. The apparatus of claim 25, the chip comprising a plurality of reactors, wherein one of the plurality of reactors comprises the predetermined reaction site.
31. The apparatus of claim 25, wherein the predetermined reaction site has a volume of less than about 500 microliters.
32. The apparatus of claim 25, wherein at least one surface of the predetermined reaction site comprises an inorganic material.
32. The apparatus of claim 25, wherein at least one surface of the predetermined reaction site comprises a polymer.
33. The apparatus of claim 25, wherein the living cell is a mammalian cell.
34. An apparatus, comprising:
a chip comprising a predetermined reaction site having a volume of less than about 1 ml;
a sensor integrally connected to the chip, wherein the sensor is able to determine an environmental factor associated with the predetermined reaction site, the environmental factor being at least one of:
pH, a concentration of a dissolved gas,
molarity, osmolarity,
glucose concentration, glutamine concentration,
pyruvate concentration, apatite concentration,
color, turbidity,

- viscosity, a concentration of an amino acid,
a concentration of a vitamin, a concentration of a hormone,
serum concentration, a concentration of an ion,
shear rate, and degree of agitation; and
- 5 an actuator integrally connected to the chip able to alter the environmental factor.
35. The apparatus of claim 34, wherein the chip is constructed and arranged to maintain at least one living cell at the predetermined reaction site.
- 10 36. The apparatus of claim 34, wherein the actuator is able to transport energy to the predetermined reaction site.
37. The apparatus of claim 36, wherein the energy comprises thermal energy.
- 15 38. The apparatus of claim 36, wherein the energy comprises sound energy.
39. The apparatus of claim 36, wherein the energy comprises mechanical energy.
- 20 40. The apparatus of claim 34, further comprising a processor able to determine a response for the actuator based on a measurement from the sensor.
41. The apparatus of claim 40, wherein the processor is integrally connected to the article.
- 25 42. The apparatus of claim 40, wherein the processor comprises an electronic circuit.
43. The apparatus of claim 34, the chip comprising a plurality of reactors, wherein one of the plurality of reactors comprises the predetermined reaction site
- 30 44. The apparatus of claim 34, wherein the predetermined reaction site has a volume of less than about 500 microliters.

45. The apparatus of claim 34, wherein at least one surface of the predetermined reaction site comprises an inorganic material.
46. The apparatus of claim 34, wherein at least one surface of the predetermined reaction site comprises a polymer.
47. The apparatus of claim 34, wherein the living cell is a mammalian cell.
48. The apparatus of claim 34, further comprising a processor able to receive a signal from the sensor and produce a signal to the actuator.
49. An apparatus, comprising:
- a chip comprising a predetermined reaction site having a volume of less than about 1 ml;
 - a first sensor integrally connected to the chip, the first sensor able to determine at least one of temperature and pressure;
 - a second sensor integrally connected to the chip, wherein the second sensor is able to determine a second environmental factor, the second environmental factor being at least one of:
 - pH,
 - molarity,
 - glucose concentration,
 - pyruvate concentration,
 - color,
 - viscosity,
 - a concentration of a vitamin,
 - serum concentration,
 - shear rate,
 - a concentration of a dissolved gas,
 - osmolarity,
 - glutamine concentration,
 - apatite concentration,
 - turbidity,
 - a concentration of an amino acid,
 - a concentration of a hormone,
 - a concentration of an ion,
 - and degree of agitation; and
 - an actuator integrally connected to the chip able to alter at least one of the temperature, the pressure, and the environmental factor.
50. The apparatus of claim 49, wherein the chip is constructed and arranged to maintain at least one living cell at the predetermined reaction site.

51. An apparatus, comprising:
- a chip comprising a plurality of predetermined reaction sites each having a volume of less than about 1 ml; and
 - a sensor able to determine an environmental factor associated with at least one of the predetermined reaction sites, the factor being at least one of:
 - CO₂ concentration,
 - glutamine concentration,
 - apatite concentration,
 - a concentration of a vitamin,
 - and a concentration of a hormone.
 - glucose concentration,
 - pyruvate concentration,
 - serum concentration,
 - a concentration of an amino acid,
52. The apparatus of claim 51, wherein the sensor is integrally connected to the chip.
53. The apparatus of claim 51, further comprising a temperature sensor.
54. The apparatus of claim 51, further comprising a pressure sensor.
55. The apparatus of claim 51, the chip comprising a plurality of reactors, wherein one of the plurality of reactors comprises the predetermined reaction site.
56. The apparatus of claim 51, wherein at least one predetermined reaction site has a volume of less than about 500 microliters.
57. The apparatus of claim 51, wherein at least one surface of at least one predetermined reaction site comprises an inorganic material.
58. The apparatus of claim 51, wherein at least one surface of at least one predetermined reaction site comprises a polymer.
59. The apparatus of claim 51, wherein the living cell is a mammalian cell.
60. The apparatus of claim 51, further comprising an actuator able to alter the environmental factor associated with at least one of the predetermined reaction sites.

61. The apparatus of claim 60, further comprising a processor able to receive a signal from the sensor and produce a signal to the actuator.
62. An apparatus, comprising:
5 a chip comprising a predetermined reaction site having a volume of less than about 1 ml; and
a control system able to produce a change in a first environmental factor associated with the predetermined reaction site within 1 s of and responsive to a change in a second environmental factor associated with the predetermined reaction
10 site.
63. The apparatus of claim 62, wherein the control system is integrally connected to the chip.
- 15 64. The apparatus of claim 62, wherein the chip is constructed and arranged to maintain at least one living cell at the predetermined reaction site.
65. The apparatus of claim 62, wherein the control system is able to produce a change in the first environmental factor within 100 ms of a change in the second
20 environmental factor.
66. The apparatus of claim 62, wherein the control system is able to produce a change in the first environmental factor within 10 ms of a change in the second environmental
25 factor.
67. The apparatus of claim 62, wherein the control system is able to produce a change in the first environmental factor within 1 ms of a change in the second environmental factor.
- 30 68. The apparatus of claim 62, the chip comprising a plurality of reactors, wherein one of the plurality of reactors comprises the predetermined reaction site.

69. The apparatus of claim 62, wherein the predetermined reaction site has a volume of less than about 500 microliters.
- 5 70. The apparatus of claim 62, wherein at least one surface of the predetermined reaction site comprises an inorganic material.
71. The apparatus of claim 62, wherein at least one surface of the predetermined reaction site comprises a polymer.
- 10 72. The apparatus of claim 62, wherein the living cell is a mammalian cell.
73. An apparatus, comprising:
a chip comprising a predetermined reaction site having a volume of less than about 1 ml; and
15 an active control system able to control an environment within the predetermined reaction site so as to support a living cell for a period of at least 1 day.
- 20 74. The apparatus of claim 73, wherein the control system is integrally connected to the chip.
75. The apparatus of claim 73, wherein the chip is constructed and arranged to maintain at least one living cell at the predetermined reaction site.